

NEUROTROPHIN RECEPTORS AND SELECTIVE LOSS OF CHOLINERGIC NEURONS IN ALZHEIMER'S DISEASE.

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Besides cortical pathology, Alzheimer's disease is also characterized by a loss of cholinergic neurons in subcortical areas. Yet, not all cholinergic neurons degenerate in Alzheimer's disease. A severe loss of cholinergic neurons is observed in the nucleus basalis of Meynert, the diagonal band of Broca, the septum and the ventral striatum. By contrast, the cholinergic neurons located in the dorsal striatum and mesencephalon are spared. Recently, it has been suspected that this differential vulnerability might be related to the presence of receptors to nerve growth factor on the most vulnerable neurons. Using antibodies raised against TrkA and TrkC, the high affinity receptors for NGF and neurotrophin-3 (NT-3), respectively, we have demonstrated the presence of TrkA and TrkC on the cholinergic neurons from the basal forebrain and on some but not all cholinergic neurons from the striatum. By contrast the mesencephalic cholinergic neurons were TrkA and TrkC-negative. In Alzheimer's disease, a loss of TrkA- and TrkC-positive neurons was observed in the nucleus basalis of Meynert. Nevertheless, the loss of 125 I-NGF binding previously reported in the striatum, no loss of TrkA-positive neurons was observed in this structure. Taken together, our results show 1) a loss of cholinergic neurons expressing TrkA or TrkC in the nucleus basalis of Meynert, 2) a survival of cholinergic neurons that do not express TrkA in the mesencephalon, 3) a possible decreased expression of TrkA in cholinergic neurons of the striatum. Whether this loss of NGF-receptors precedes neuronal loss remains to be demonstrated.